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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
HUI, SAN MING R	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/750,878
Filing Date: January 05, 2004
Appellant(s): EGGENWEILER ET AL.

Harry Shubin
Millen, White, Zelano & Branigan, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, VA 22201
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 12, 2006 appealing from the Office action mailed January 10, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Carter et al., Chemotherapy of Cancer 2nd ed. 1981, pages 362-365

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not provide sufficient information that all tumors are treatable by the herein claimed compounds described in the methods claimed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the

claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) **The nature of the invention**

All of the rejected claims are drawn to an invention which pertains to a method of treating mammals with variously substituted benzopyrano-imidazole compounds for the inhibition of tumor growth. The nature of the invention is complex in that it encompasses the treatment of all types of tumors.

(2) **Breadth of the Claims**

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass inhibition of any number of tumors by the herein claimed benzopyrano-imidazole compounds.

(3) **Guidance given by the instant specification**

The guidance given by the specification as to how one would administer the herein claimed compounds to a subject in order to inhibit any type of tumor growth is limited. All of the guidance provided by the specification is directed toward the possibilities of treating tumor by PDE IV inhibitors (See the instant specification, page 3, lines 30-33). The instant specification does not mention of how PDE VII be able to be used as anti-tumor agents. Examiner notes that "the instant specification states that PDE VII inhibitors may also inhibit the growth of tumor cells" [emphasis added].

(4) **Working Examples**

There is no working example disclosed in the instant specification.

(5) **State of the Art**

While the state of the art is relatively high with regard to treating specific cancers or tumors, the state of the art with regard to treating cancer or tumor generally is underdeveloped. In particular, there is no known anticancer agent which is effective against all cancers. Carter et al. (Chemotherapy of Cancer 2nd ed 1981) clearly teaches that for the forty known anticancer agents, none are effective against all cancers (pages 362-365). There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-I), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Even those that affect a single organ are often not generally treatable. For example, the main types of lung cancer are small cell (oat cell), giant cell, clear cell, adenocarcinoma of the lung, squamous cell cancer of the lung, and mesothelioma. There is no such thing as a treatment of these generally because of their diversity. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

(6) **Predictability of the Art**

The invention is directed to inhibiting tumor growth in general. It is well established that "the scope of enablement various inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970). Cancers are especially unpredictable due to their complex nature. Please refer to the discussion of Carter, et al. and the state of the art in (5) that shows the different treatments of cancers. The treatment of one type of cancer or tumor could not be necessarily the same for the other type.

(7) **The Quantity of Experimentation necessary**

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for inhibiting cancer cells. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding treatment of cancer with any herein claimed compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding treatment of cancer with

any compound, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of cancer because, as described by Carter, et al., there is no known drug effective for inhibiting all types of cancer. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to inhibit cancer cells in a mammal by administration of one of the compounds within the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for inhibiting tumor growth generally by administering the herein claimed various benzopyrano-imidazole compounds is not considered to be enabled by the instant specification.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for rheumatoid arthritis, multiple sclerosis, Crohn's disease, diabetes mellitus, and ulcerative colitis, does not reasonably provide enablement for other autoimmune disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the specification fails to provide information that would allow the skilled artisan to fully

practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) **The nature of the invention**

All of the rejected claims are drawn to an invention which pertains to a method of treating mammals with variously substituted benzopyrano-imidazole compounds for the treatment of autoimmune disorders. The nature of the invention is complex in that it encompasses the treatment of all types of autoimmune disorders.

(2) **Breadth of the Claims**

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass inhibition of any number of autoimmune disorders, whether they are mediated by TNF-α or not, by the herein claimed benzopyrano-imidazole compounds.

(3) **Guidance given by the instant specification**

The guidance given by the specification as to how one would administer the herein claimed compounds to a subject in order to inhibit any type of autoimmune

disorders is limited. All of the guidance provided by the specification is directed toward the possibilities of treating autoimmune disorders by PDE VII inhibitors because of its TNF-α inhibitory effect (See the instant specification, page 3, lines 8-15).

(4) **Working Examples**

There is no working example disclosed in the instant specification.

(5) **State of the Art**

While it is known that some drugs are useful for treating multiple autoimmune diseases, other drugs are not as versatile. Christodoulos et al. teaches that minocycline can be used to treat rheumatoid arthritis, but can also lead to drug-induced lupus, another autoimmune disease for example (Chest. 1999;115(5): 1471).

(6) **Predictability of the Art**

Multiple claims are directed to treatment of autoimmune conditions in general. It is well established the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiology activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833,839 (1970. The art is unpredictable because the treatment of one type of autoimmune condition will not necessarily be the same for the other type.

(7) **The Quantity of Experimentation necessary**

In order to practice the claimed invention, one of skill in the ad would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One

would then need to test the combination in the model system to determine whether or not the combination is effective for decreasing the amount of therapeutic agent needed to treat an autoimmune disease. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding sparing the amount of therapeutic agent administered to a. patient with an autoimmune disease by administering a sleep restorative agent, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compounds, compound dosage, duration of treatment, route of administration, etc. and appropriate model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of an autoimmune disease, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of autoimmune disease because, as shown by Christodoulos et al., some drugs will not necessarily treat all types of autoimmune conditions. Therefore, it would require undue experimentation to practice the claimed invention of decreasing the effective amount of a recited therapeutic agent administered to a subject having an autoimmune condition by administering the benzopyrano-imidazole agent recited in the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for inhibiting tumor growth generally by administering the herein claimed various benzopyrano-imidazole compounds is not considered to be enabled by the instant specification.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not provide sufficient information that memory disturbances are treatable by the herein claimed compounds described in the methods claimed.

The specification does not provide sufficient information that all tumors are treatable by the herein claimed compounds described in the methods claimed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the

claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) **The nature of the invention**

All of the rejected claims are drawn to an invention which pertains to a method of treating mammals with variously substituted benzopyrano-imidazole compounds for the treatment of memory disturbances. The nature of the invention is complex in that it encompasses the treatment of all types of memory disturbances.

(2) **Breadth of the Claims**

The claims are so broad that they encompass any mental status changing disorder that could potentially affect CNS.

(3) **Guidance given by the instant specification**

There is no guidance as to how PDE VII inhibitors related to memory disturbances. No guidance as o how to treat such disorders is disclosed.

(4) **Working Examples**

There is no working example disclosed in the instant specification.

(5) **State of the Art**

It is known in the art the herein claimed benzopyrano-imidazole compounds as CNS depressants (See the abstract of Savel'ev et al. Khimiko-Farmatsevticheskii Zhurnal, 1993;17(6):697-700), which is a sedative agent. Sedative agent will generally cause memory disturbances rather than treating the same.

(6) **Predictability of the Art**

Multiple claims are directed to treatment of autoimmune conditions in general. It is well established the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiology activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833,839 (1970).

(7) **The Quantity of Experimentation necessary**

In order to practice the claimed invention, one of skill in the art would have to first envision the use of a sedative agent, which is commonly causing memory disturbance, to treat memory disturbance. There is no guidance in the instant specification to the one of skilled in the art as to how to go by employing a contradictory effect for treatment.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for inhibiting tumor growth generally by administering the herein claimed various benzopyrano-imidazole compounds is not considered to be enabled by the instant specification.

(10) Response to Argument

Appellant's arguments in the Brief filed September 12, 2006 averring the instant specification meets the requirements of rejection under 35 USC 112, first paragraph are unconvincing. Appellant argues that since the instant compounds have antagonistic

effect on the production of TNF alpha, and thus are useful to treat all immune diseases (See page 4 of the Brief filed September 12, 2006). Such arguments are not convincing. Firstly, it is not at all clear how PDE VII inhibitors would be able to block TNF alpha. Even though *arguendo* that the instant compounds have antagonistic effect on the production of TNF alpha, it is still not clear how such compounds can have effect on all immune disorders. It is well-known that human immune system is very complex and in order to be useful to treat all immune diseases, such agent would have modulating activity on all of the immune systems and subsystems. It is also known in the art that not a single agent or compound could have interact with every facet of the immune systems, subsystems, cascades, and pathways, let alone modulating them. Examiner notes that TNF alpha is one of the many factors that exist in human immune systems. Subsequently, it is not clear how blocking the effect or production of TNF alpha could lead to treatment for all of the immune diseases. Furthermore, the instant specification so lack of guidance and rationales that the instant compounds, being PDE VII inhibitors, could have affected all of the immune systems. Therefore, one of skilled in the art would have to perform undue experimentation to practice the full scope of the herein claimed invention.

Appellant's arguments in pages 4-5 of the Brief filed September 12, 2006 averring Appellant's specification clearly enables one to make and use the disclosed compounds in the claimed methods since the Examiner has not provided any evidence for supporting Examiner's position that the herein claimed invention as not enabled are not convincing. As discussed in the previous office actions mailed 1/10/2006 and

7/14/2005, evidences have been provided in Carter casting doubts on the truth of what is claimed that no known single magic bullet is effective for treating all of the tumors. Furthermore, the instant specification does not even provide any guidance as to PDE VII inhibition in relation to the treatment of tumor growth and/or metastasis. It is known that different tumor types are essentially very different diseases. For example, solid tumor (e.g., heptocellular carcinoma) is very different from non-solid tumor (e.g., leukemia) in terms of etiology, pathophysiology, treatment, prognosis, clinical symptoms, etc. Therefore, even considered the skill of skilled artisan possesses, the instant specification still not providing sufficient information as to how to practice the full scope of the claims.

Appellant's arguments in pages 6-7 in the Brief filed September 12, 2006 averring the mere discussion of the factors in *Wands supra* as insufficient; rather the Office has to furnish reasons or evidences are not convincing. In order to determine whether the instant claims are enabled for its full scope, the Examiner had discussed the eight factors clearly in the previous office action. There are sufficient reasons to show that the instant claims do not meet the requirements of 35 USC 112, first paragraph. In view of the discussion with provided evidence, the skilled artisan would have to perform undue experimentation to find out what is working and what is not as to the treatment of tumor growth and metastasis. In the discussion above, Examiner not only casting doubt on the inoperability of the invention. Examiner believes that the previous office actions have discussed the eight factors of *Wands supra* in addition to questioning the inoperability of the invention. Furthermore, Examiner also provided

evidence showing that the state of the art does not even recognize the possibility of a single active agent to interact different tumor types, let alone treating all of them. When turning to the instant specification for guidance, the specification is lacking the information for selecting and ascertaining the type of diseases the instant compounds might be effective against. As for the remarks with regard to autoimmune diseases, Examiner notes that it is well-known in the art that autoimmune diseases there are various disorders with different etiology, deposition factors, treatment, or pathophysiology. The instant specification only shows certain autoimmune diseases in the instant specification. Other than the disorders discussed in the instant specification, it would require undue experimentation to test the herein claimed compounds for various autoimmune diseases to practice the full scope of the instant invention.

Appellant's arguments in page 7 of the Brief filed September 12, 2006 with regard to the breath of the claims are unconvincing. Examiner notes that it is not the compounds recited being broad; rather it is the disease states recited are so broad that they represent a vast array of disorders without any art-recognized central pathophysiology or etiology. Furthermore, as discussed above, the compounds are used as PDE VII inhibitors; however, the instant specification never discloses how the blocking of PDE VII would be effective in treating such vast array of disorders. Accordingly, the instant claims are considered properly rejected under 35 USC 112, first paragraph. Examiner further notes that in page 7 of the Brief, Appellant states, "With respect to the state of the art, PDE inhibitors are well known to be implicated in signaling pathways which are instrumental in the formation of tumors". Such statement

is not supported by any references of record. It is noted that such statement is over-simplify the matters and further it has nothing to do with PDE VII. Examiner notes that other PDE enzyme may be related to the formation of tumor. There is no evidence of record that pointed to PDE VII as related to tumor growth. Even if it is, from the evidence provided by the Examiner, i.e., Carter, it is clear that the instant compounds are not enabled for the full scope of the claims.

Appellant's arguments in page 8 of the Brief filed September 12, 2006 with regard to Carter are unconvincing. As discussed above, it is so clear that not even a single class of compound would have interacted with all and every type of tumor regardless of the nature of interaction tested in Carter, let alone treating all types of tumor. Appellant clearly misunderstands and mischaracterizes the reason why Carter was cited in the rejection in the previous office action mailed 7/14/2005. The issue at hand is that whether one of skilled in the art would have to perform undue experimentation to make and use the instant compounds for treating all of the recited diverse disorders. In the instant case, the instant specification does not enable one of skilled in the art to select, screen, and test the compounds for treating all of the disorders recited. Accordingly, the claims are considered as properly rejected under 35 USC 112, first paragraph.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

San-ming Hui
Primary Examiner
Art Unit 1617

SHAOJIA ANNA JIANG, PH.D.
SUPERVISORY PATENT EXAMINER

Conferees:

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER